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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,056	12/11/2000	Leonard Katz	4952.US.C1	4609
23492	7590	10/19/2005	EXAMINER	
ROBERT DEBERARDINE ABBOTT LABORATORIES 100 ABBOTT PARK ROAD DEPT. 377/AP6A ABBOTT PARK, IL 60064-6008			MOORE, WILLIAM W	
			ART UNIT	PAPER NUMBER
			1656	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,056

Applicant(s)

KATZ ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59,61,73-75,79-81 and 84 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59,61,73-75,79-81 and 84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Terminal Disclaimer and Amendment

Applicant's Terminal Disclaimer filed 25 July 2005 is accepted and effective in obviating the obviousness-type double patenting rejection of record of claims herein over claim 1 of US Patent No. 6,004,787. Applicant's Amendment filed 25 July 2005, canceling claim 72 and amending claims 73, 79 and 84, uses terms proposed in the communication mailed 22 March 2005 but a new ground of rejection under 35 U.S.C. § 112, first paragraph, is stated herein thus this communication is not made final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 61, 73-75, 79-81 and 84 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of biosynthesis of modified polyketides by host cells transformed with an altered polyketide synthase-encoding DNA sequences **endogenous to a transformed host cell wherein the polyketide is produced by a process of homologous recombination**, does not reasonably provide enablement for methods of biosynthesis of modified polyketides by host cells wherein polyketide synthase-encoding DNA sequences are heterologous to a transformed host cell that does not produce the same or a related polyketide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

Applicant's amendments of 25 July 2005 prompt reconsideration of the scope of the claims. It was previously agreed that the specification, in view of the prior art of record, enables the identification of enolyreductase-, ketoreductase-, and dehydratase-specifying regions of actinomycete PKS-encoding DNA sequences and their subsequent disruption within, or addition to the DNA sequences encoding a module of an actinomycete polyketide synthase. It is also agreed

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that productive transformation of a host cell other than the cell that is the source of the gene encoding the polyketide synthase before its alteration can be effected by replacing a native PKS gene with the altered polyketide synthase-encoding DNA sequence by recombination to provide a suitable context for expression by a heterologous host cell when integrated into the chromosome of that host cell. Yet the claims are not limited to the expression of an altered polyketide synthase that is integrated by recombination in the chromosome of a host cell and neither the specification nor the prior art of record herein teach how a generic, heterologous, host cell may survive the practice of a claimed method after transformation. Claims 59, 61, 73-75, 79-81 and 84 are rejected because the claims embrace methods of producing modified polyketides by transforming an actinomycete host cell with a modified DNA sequence that does not become integrated into the chromosome of the host cell, the sole process disclosed in both the earliest parent application serial No. 07/642,734 and the continuation-in-part application serial No. 08/858,083 of which the instant application is a divisional filing. Both the prior art of record and the instant specification, see, e.g., page 1 line 35, teach that many polyketides are toxic compounds - either anti-microbial or anti-fungal - for unicellular organisms. There is no suggestion or teaching in the specification of how to protect a prospective host cell from the toxic effects of a modified polyketide produced after transformation of the host cell according to a claimed method when the polyketide produced is unrelated structurally to a polyketide the host cell itself produces, or if the host cell itself produced no polyketide. It is well settled that the first paragraph of 35 U.S.C. § 112 requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor

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supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing eight factors relevant to analysis of enablement). Applying the analysis discussed in *Wands* to Applicant's disclosure, it is apparent that:

the specification lacks adequate, specific, guidance for practicing a claimed method with transformed host cells susceptible to the toxic effects of a modified polyketide to be prepared other than by chromosomal integration by homologous recombination,

the specification lacks working examples wherein a cell susceptible to the toxic effects of a modified polyketide to be prepared according to the method is transformed with a modified, heterologous, polyketide synthase-encoding DNA sequence and survives the production of the modified polyketide other than by chromosomal integration by homologous recombination,

in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support the practice a claimed method with transformed host cells susceptible to the toxic effects of a modified polyketide to be prepared according to a method other than chromosomal integration by homologous recombination, and,

unpredictability exists in the art where no *Actinomycetales* are demonstrated to support the production of altered polyketides other than by expression of altered DNA sequences integrated in the cell's chromosome by homologous recombination.

Thus the scope of methods practiced according to clause (4) of claim 84 providing for, "transforming a polyketide-producing *Actinomycetales* cell with the altered polyketide-encoding DNA sequence to replace a native polyketide-encoding DNA sequence of the microorganism" are neither described in the specification nor shown to be effective absent chromosomal integration by homologous.

Conclusion

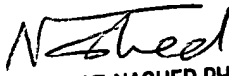
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is

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571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for communications to the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
14 October 2005


NASHAAT T. NASHED PHD.
PRIMARY EXAMINER